66. (New) The method of claim 65, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

67. (New) The method of claim 65, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

E1 Cont

68. (New) The method of claim 67, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

69. (New) The method of claim 67, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

70. (New) The method of claim 69, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

71. (New) The method of claim 63, wherein the cell is a 293 cell.

72. (New) The method of claim 63, wherein the cell is an A549 cell.

REMARKS

The Present Invention

The present invention provides a plasmid comprising a reading frame ORF6 of an E4 region of an adenovirus genome under the control of a heterologous inducible promoter. The present invention also provides a defective recombinant adenovirus that (a) requires, for replication, complementation *in trans* of one or more essential gene functions of an E1 region and an E4 region of an adenovirus genome, and (b) comprises an adenoviral genome wherein all or part of the E1 region and the whole of the E4 region, and optionally all or part of the E3 region, is deleted from the adenoviral genome. The present invention further provides a system and method useful for propagating a replication-deficient adenoviral vector.

The Pending Claims

Upon entry of this amendment, claims 44 and 48-72 will be pending. Separate documents setting forth the precise changes to the claims, as well as the text of the pending claims, are submitted herewith.

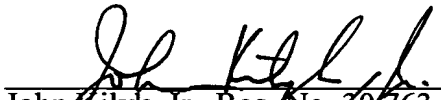
The Amendments to the Claims

Claims 44 and 48-52 are discussed in the "Response to Office Action" dated October 11, 2002, the entry of which is requested by way of the accompanying Request for Continued Examination (RCE). By way of this "Supplemental Response to Office Action," claims 53-72 have been added. Claims 53-62 are directed to a system comprising a multiply replication-deficient adenoviral vector and a complementing cell line that is a 293 cell or an A549 cell. Claims 63-72 are directed to a method of propagating a multiply replication-deficient adenoviral vector and parallel claims 53-62. Claims 53-62 and claims 63-72 refer to specific cell lines (i.e., 293 and A549) but otherwise parallel claims 69-73 and claims 74-78, respectively, of copending Application No. 09/321,797. Support for claims 53-72 can be found in the specification at, for example, page 11, lines 26-31, page 13, line 4 - page 14, line 17, and Examples 3, 4, and 8-11. Accordingly, no new matter has been added by way of these new claims.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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CERTIFICATE OF MAILING

I hereby certify that this SUPPLEMENTAL RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: November 14, 2002

PATENT
Attorney Docket No. 213257

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Kovesdi et al.

Application No. 09/964,065

Art Unit: 1632

Examiner: S.D. Priebe

Filed: September 26, 2001

For: REPLICATION-DEFICIENT ADENOVIRAL VECTOR AND PLASMID WITH ADENOVIRAL COMPONENT

AMENDMENTS TO CLAIMS

Amendments to existing claims:

53. (New) A system comprising:

(i) an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome, and

(ii) a 293 cell or an A549 cell having a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome,

wherein there is no overlap between the cellular genome and the adenoviral genome to mediate a recombination event between the cellular genome and the adenoviral genome.

54. (New) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

55. (New) The system of claim 53, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1

region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions of the E4 region of the adenoviral genome.

56. (New) The system of claim 55, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

57. (New) The system of claim 55, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

58. (New) The system of claim 57, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

59. (New) The system of claim 57, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

60. (New) The system of claim 59, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

61. (New) The system of claim 53, wherein the cell is a 293 cell.

62. (New) The system of claim 53, wherein the cell is an A549 cell.

63. (New) A method of propagating an adenoviral vector, which method comprises

(a) providing an adenoviral vector comprising an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions in either or both of the E2A

region and the E4 region of the adenoviral genome, and optionally a deficiency in the E3 region of the adenoviral genome,

(b) providing a 293 cell or an A549 cell comprising a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in either or both of the E2A region and the E4 region of the adenoviral genome, wherein there is no overlap between the cellular genome and the adenoviral genome to mediate a recombination event between the cellular genome and the adenoviral genome, and

(c) propagating the adenoviral vector in the cell.

64. (New) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

65. (New) The method of claim 63, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and a deficiency in one or more essential gene functions of the E4 region of the adenoviral genome, and the cell has a cellular genome that complements in *trans* for the deficiency in one or more essential gene functions of the E1 region of the adenoviral genome and the deficiency in one or more essential gene functions in the E4 region of the adenoviral genome.

66. (New) The method of claim 65, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

67. (New) The method of claim 65, wherein the cellular genome comprises at least open reading frame (ORF) 6 of the E4 region of the adenoviral genome.

68. (New) The method of claim 67, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

69. (New) The method of claim 67, wherein the cellular genome comprises at least ORF6 and no other ORF of the E4 region of the adenoviral genome.

70. (New) The method of claim 69, wherein the adenoviral vector comprises an adenoviral genome having a deficiency in all essential gene functions of the E1 region, and the cell has a cellular genome that complements in *trans* for the deficiency in all essential gene functions of the E1 region.

71. (New) The method of claim 63, wherein the cell is a 293 cell.

72. (New) The method of claim 63, wherein the cell is an A549 cell.